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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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09/424,519    03/03/00    MITCHELL    J    175931

LEYDIG VOIT & MAYER  
180 NORTH STETSON  
TWO PRUDENTIAL PLAZA SUITE 4900  
CHICAGO IL 60601-6780

HM22/0130

EXAMINER

KWON, B

ART UNIT

PAPER NUMBER

1614

DATE MAILED:

01/30/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

<b>Office Action Summary</b>	Application No. 09/424,519	Applicant(s) MITCHELL ET AL.	
	Examiner Brian-Yong S Kwon	Art Unit 1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondenc address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 03 March 2000.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 4-21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 22-27 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claims \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

#### Attachment(s)

- |   |  |
|---|--|
| 15) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 18) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 16) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 19) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 17) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>1</u> | 20) <input type="checkbox"/> Other:  |

**DETAILED ACTION*****Election Acknowledged***

Applicants election of species, the 4-hydroxy-2,2,6,6,-tetramethylpiperidine-1-oxyl (Tempol), is acknowledged. Claims 4-21 are withdrawn from further consideration by the examiner, 27 CFR 1.142 (b), as being drawn to a non-elected invention, the requirement having been traversed in Paper No. 6.

Applicant's remarks are noted but a claimed nitroxide compounds of formula I or II (e.g., Tempol) are known compounds in the art, therefore, the inventions would lack unity since the compounds are not applicants contribution over the prior art. The species lack the same or corresponding special technical feature. In addition, the use of nitroxides (e.g., Tempol) are not only limited to the context of the instant claimed method in the treatment of cancer. Nitroxides have been used in preventing or treating different types of conditions including cataracts (US 6001853), ischemic cell damage (WO 88/05044), photaging and other type of sun damage (US 5840734) and hair loss and stimulation of hair growth (US 5716947), and in medical imaging (US 5840701).

In view of above, it would be burdensome to search all of different methods in different databases. Additionally, the different heterocyclic group would support separate patents.

Applicant traverses on the grounds that the election requirement does not comply with PCT restriction practice. The election requirement has been restated above to state the rationale under the relevant PCT standards. The examiner is not precluded from asserting election requirement in the national stage even though no restriction was required in the PCT examination. Applicants argue that no restriction is proper because "there is a single general

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inventive concept-the use of a nitroxide (or prodrug thereof) in the treatment of cancer” and “the special technical feature of the compounds used in the treatment of cancer in accordance with the present invention is that the compounds are nitroxides (and prodrugs thereof)”. This argument is not persuasive, however. Only an election of species requirement has been issued. As Applicant’s arguments to the contrary are not persuasive, and extreme burden of search would exist were the election not required, the election requirement shall be maintained- and is hereby made Final.

The claims are being examined wherein R1 is O, each of R2, R3, R4 and R5 is methyl(a C1-20 alkyl group), N=1, one of R6 and R7 is hydrogen and the other is hydroxy, and each of R8-R11 is hydrogen.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1-3, 22, 24 and 26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the specific cancer by regulating the specific tumor suppressor gene such as p53, does not reasonably provide enablement for the term “a cancer” and “a genetic defect of a cancer regulatory gene or a tumor suppressor gene”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The treatment of cancer art remain highly unpredictable, and no examples exist for efficacy of a single product against all types of claimed conditions or diseases generally.

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Therefore, based on the unpredictable nature of the invention and state of the prior art, the lack of guidance and working examples, and the extreme breadth of the claims, one skilled in the art could not use the entire scope of the claimed invention without undue experimentation.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Monti et al.

(PAACR Annual Meeting, vol.36, no. 0, 1995).

Monti et al. teach that “the stable nitroxide Tempol... act as radioprotector in mice”. The reference clearly anticipates the prophylactic use of claimed invention. It is now well settled law that administering compounds or composition inherently possessing a protective utility anticipates claims directed to such protective use. See *Ex parte Novitski* 126 USPQ 1389 (BOPA 1993).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Monti et al. (PAACR Annual Meeting, vol. 38, no. 0, 1997) in view of Harris et al. (J. Natl Cancer Inst 1996;88;1442-55).

Claims read on a method for the prophylactic or therapeutic treatment of cancer in an animal with a pharmaceutical composition comprising Tempol.

Monti et al. (PAACR Annual Meeting, vol. 38, no. 0, 1997) teach that a cytotoxicity of Tempol in human leukemic cells is related to induction of apoptosis.

Harris et al. (J. Natl Cancer Inst 1996;88;1442-55) teach that many of human cancers harbors p53 mutations; the high frequency of p53 mutations in human cancers attests to its

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importance as a target of rational cancer therapy; many of the currently successful cancer therapeutic agents inhibit tumor growth by increasing the rate of tumor cell death by apoptosis; and cells exposed to agents that produce DNA damage, such as double-strand breaks, frequently use the p53-mediated pathway of apoptosis. See from page 10 lines 41 to page 11 line 1 as well from page 12 line 13-16.

The teaching of Monti et al. differs from the claimed invention in the chemotherapeutic effect of Tempol in vivo; and the use of Tempol for treating cancer that is due to p53 mutation.

It would have been obvious to a person skilled in the art to modify the Monti et al.'s teaching such that Tempol is administered to animal including human to treat cancer. One having ordinary skilled in the art would have expected an anticancer effect of Tempol in vivo. Furthermore, one having ordinary skilled in the art would have been motivated to treat cancer associated with a genetic defect of p53 tumor suppressor gene taught by Harris et al. because both references teach that the inhibition of tumor growth by apoptosis is important in cancer treatment.

### ***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Kwon whose telephone number is (703) 308-5377. The examiner can normally be reached Monday through Friday from 8:00am to 4:30pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mariann Cintins, can be reached on (703) 308-4725. The fax number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

Brian Kwon

**ZOHREH FAY**  
**PRIMARY EXAMINER**  
GROUP 1600

